PATENT SPECIFICATION (11) 1358915

(21) Application No. 42625/71 (22) Filed 13 Sept. 1971
(44) Complete Specification published 3 July 1974
(51) International Classification A61J 3/06 A61K 9/00
(52) Index at acceptance
B5A 1R9
A5B 730 731 733 734 73Y 750 751 75Y 764
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1358915

(54) DIRECTLY COMPRESSED TABLET AND COMPOSITION THEREFOR

(71) We, MERCK & CO. INC., a corporation duly organised and existing under the laws of the State of New Jersey, United States of America, of Rahway, New Jersey, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to edible tablets, particularly pharmaceutical tablets containing biologically active agents such as vitamins, minerals, nutrients or drugs or their mixture.

Almost all biologically active agents of crystalline or powdered material have to be put through either a so-called dry granulation series of steps or a wet-granulation series of steps to obtain a composition that can be compressed into satisfactory tablets. A simple mixture of the active agents with the usual pharmaceutical binders, diluents and lubricants can be compressed directly into a tablet but they may not possess the desired strength and resistance to shock. To obtain a satisfactory tablet the tablet forming composition has required a preliminary formation into granules of predetermined size.

The dry granulation process requires that the tablet forming mixture first be compressed into large hard slugs under high pressures. Those slugs are then reduced to a granular size which can then be recompressed to a finished tablet in a conventional tablet compression machine. This granulation operation is costly because it requires expensive machines, working space and labor and because the several steps involve a considerable time.

The wet granulation process similarly has its drawbacks. It first involves mixing the tablet ingredients and then their wetting with a liquid such as water, alcohol or other organic solvent. This properly wetted preparation is then dried in an oven and the solid compacted mass is reduced into granules of the proper size for tableting in a tablet compression machine. This entire process, like the dry granulation process, requires high priced apparatus, liquids that may be expensive, skilled workmen and considerable time, all of which adds to the high cost of the tablets.

In accordance with the present invention, tablets containing a biologically active agent are made by encapsulating particles of the said agent with a coating material permeable to stomach or intestinal fluids and having chemical groups that are subject to intermolecular bonding forces, and compacting a body of the encapsulated particles into a tablet without a preliminary granulation process.

The present invention by-passes all of the intermediate steps of the wet and dry granulation processes as the tableting mixture is directly supplied to the tableting machine and tablets are obtained; hence, this is referred to as a direct compression process, which term is to be understood as meaning that the granulation steps are omitted and the tableting mixture is directly supplied to the tableting machine. The invention is based on the discovery that this direct compression process is made possible if the active agent has been microencapsulated in a coating material in accordance with known techniques.

Although the technical reason for the direct compressibility feature of microencapsulated agents is not fully understood a possible explanation is that the coating materials are all subject to intermolecular bonding forces. These forces arise from groups such as hydroxyl, carboxyl and amino in the chemical compounds of the coating materials. The compaction of the materials in the tableting machine apparently causes these intermolecular bonding forces to exert their cohering effect and bind the tablet together.

This invention contemplates the use of any microencapsulated solid biologically active agent to make tablets by direct compression. These agents include vitamins, powdered iron